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Metal−Organic Frameworks for Analytical Chemistry: From Sample Collection to Chromatographic Separation

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CONSPECTUS

In modern analytical chemistry researchers pursue novel materials to meet analytical challenges such as improvements in sensitivity, selectivity, and detection limit. Metal−organic frameworks (MOFs) are an emerging class of microporous materials, and their unusual properties such as high surface area, good thermal stability, uniform structured nanoscale cavities, and the availability of in-pore functionality and outer-surface modification are attractive for diverse analytical applications. This Account summarizes our research on the analytical applications of MOFs ranging from sampling to chromatographic separation.

MOFs have been either directly used or engineered to meet the demands of various analytical applications. Bulk MOFs with microsized crystals are convenient sorbents for direct application to in-field sampling and solid-phase extraction. Quartz tubes packed with MOF-5 have shown excellent stability, adsorption efficiency, and reproducibility for in-field sampling and trapping of atmospheric formaldehyde. The 2D copper(II) isonicotinate packed microcolumn has demonstrated large enhancement factors and good shape- and size-selectivity when applied to on-line solid-phase extraction of polycyclic aromatic hydrocarbons in water samples. We have explored the molecular sieving effect of MOFs for the efficient enrichment of peptides with simultaneous exclusion of proteins from biological fluids. These results show promise for the future of MOFs in peptidomics research. Moreover, nanosized MOFs and engineered thin films of MOFs are promising materials as novel coatings for solid-phase microextraction. We have developed an in situ hydrothermal growth approach to fabricate thin films of MOF-199 on etched stainless steel wire for solid-phase microextraction of volatile benzene homologues with large enhancement factors and wide linearity.

Their high thermal stability and easy-to-engineer nanocrystals make MOFs attractive as new stationary phases to fabricate MOF-coated capillaries for high-resolution gas chromatography (GC). We have explored a dynamic coating approach to fabricate a MOF-coated capillary for the GC separation of important raw chemicals and persistent organic pollutants with high resolution and excellent selectivity. We have combined a MOF-coated fiber for solid-phase microextraction with a MOF-coated capillary for GC separation, which provides an effective MOF-based tandem molecular sieve platform for selective microextraction and high-resolution GC separation of target analytes in complex samples.

Microsized MOFs with good solvent stability are attractive stationary phases for high-performance liquid chromatography (HPLC). These materials have shown high resolution and good selectivity and reproducibility in both the normal-phase HPLC separation of fullerenes and substituted aromatics on MIL-101 packed columns and position isomers on a MIL-53(Al) packed column and the reversed-phase HPLC separation of a wide range of analytes from nonpolar to polar and acidic to basic solutes. Despite the above achievements, further exploration of MOFs in analytical chemistry is needed. Especially, analytical application-oriented engineering of MOFs is imperative for specific applications.
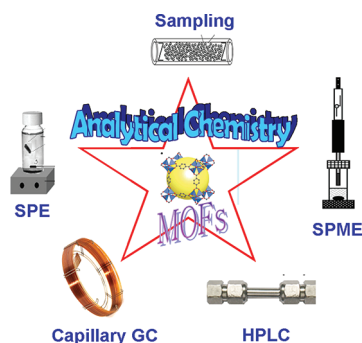
Introduction

Novel advanced materials have received great interest in modern analytical chemistry because of their potential analytical applications. Metal−organic frameworks (MOFs) are a new class of hybrid inorganic−organic microporous crystalline materials self-assembled straightforwardly from metal ions with organic linkers via coordination bonds. The availability of various building blocks of metal ions and

TABLE 1. Characteristic Data and Analytical Applications of Several MOFs

MOFs	formula	characteristic data[11−13,18,21−26,29,31−36]						analytical applications
		BET surface area ($m^2 g^{-1}$)	pore/channel diameter (Å)	window diameter (Å)	open metal sites	thermostability (°C)	moisture stability	
MOF-5, IRMOF-1	$Zn_4O(BDC)_3$, BDC = terephthalic acid	630−2900	11, 15	7.5, 11.2	no	400−480	no	sorbent for sampling and trapping,[11,12] stationary phase for GC,[23,25,28,29] chromatography on a single MOF-5 crystal[41]
copper(II) isonicotinate	$Cu(4\text{-}C_5H_4N\text{-}COO)_2(H_2O)_4$	146			no		yes	sorbent for SPE of PAHs in water[14]
	Gd(DPA)(HDPA), DPA = pyridine-2,6-dicarboxylicate						yes	sorbent for SPE of pesticides[15]
	$(La_{0.9}Eu_{0.1})_2(DPA)_3(H_2O)_3$						yes	sorbent for SPE of pesticides[16]
IRMOF-3	$Zn_4O(NH_2{-}BDC)_3$	1957		9.6	no	320	no	stationary phase for GC[25]
HKUST-1, MOF-199	$Cu_3(BTC)_2$, BTC = 1,3,5-benzenetricarboxylate	1000−1458	12	8, 9	yes	280	no	engineered films for SPME,[19,29] stationary phase for LC[33,37]
MIL-47(V)	$V^{IV}O(BDC)$	800	8.5	8.5	no	350	yes	stationary phase for GC[21] and LC[31]
MIL-53(Al)	$Al^{III}(OH)(BDC)$	940−1038	8.5	8.5	no	330	yes	sorbent for enriching peptides and removing proteins,[18] stationary phase for LC[32,35,39]
MIL-100(Cr)	$Cr_3O(H_2O)_2F(BTC)_2$	1595	25, 29	5.6, 8.6	yes	350	yes	sorbent for enriching peptides and removing proteins[18]
MIL-101(Cr)	$Cr_3O(H_2O)_2F(BDC)_3$	2736−2907	29, 34	12, 16	yes	300−330	yes	engineered films for QCM,[13] sorbents for enriching peptides and removing proteins,[18] stationary phase for GC[24,29] and LC[34,36]
ZIF-7	$Zn(benzimidazolate)_2$		4.3	2.9	no	480	yes	engineered films for SPME,[29] stationary phase for GC[26,29]
ZIF-8	$Zn(2\text{-methylimidazole})_2$	1504	11.4	3.4	no	380−550	yes	engineered films for SPME,[29] sorbent for μ-SPE,[17] stationary phase for GC[22,26,29]

organic linkers makes it possible to prepare an infinite number of new MOFs with diverse structures, topologies, and porosity.[1−4] Owing to their fascinating structures and unusual properties, such as permanent nanoscale porosity, high surface area, good thermostability, and uniform structured cavities, MOFs have great potential for diverse applications, such as hydrogen storage, gas separation, catalysis, sensing, and bioimaging.[5−10]

The diverse structures and unique properties also make MOFs attractive for analytical applications (Table 1, Figure 1).[11−41] Recently, great efforts have been made in our laboratory to explore MOFs for analytical chemistry. MOFs have been either directly used or engineered to meet the analytical challenges in sample collection, preconcentration, extraction, and chromatographic separation to improve sensitivity, selectivity, and detection limit. This Account summarizes our research on the analytical applications of MOFs. Specifically, five analytical applications of MOFs have been explored in our laboratory: (1) bulk microsized MOFs as sorbents for in-field sampling and solid-phase extraction (SPE);[12,14,18] (2) nanosized MOFs and engineered thin films of MOFs as coatings for solid-phase microextraction (SPME), quartz crystal microbalance (QCM), and matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF-MS);[13,18,19] (3) MOFs as stationary phases for high-resolution gas chromatography (GC);[24−26,29] (4) MOF-based tandem molecular sieve platform for selective extraction and high-resolution GC;[29] (5) microsized solvent-resistant MOFs as stationary phases for high-performance liquid chromatography (HPLC).[34−36,39]

MOFs for In-Field Sampling and Adsorption

Volatile organic compounds (VOCs) are a major group of air pollutants; development of good materials for efficient sampling and trapping of VOCs is thus significant in environmental and analytical sciences. With large surface area and high thermostability, MOFs have great potential as sorbents for sampling and enriching VOCs before GC−MS analysis. Although IRMOF-1 has been used as sorbent for trapping standard dimethyl methylphosphonate (DMMP) gas for thermal desorption (TD) GC−MS, no such application to real sample analysis have been reported.[11] Recently, we have explored a MOF-5 packed quartz tube for in-field sampling and preconcentration of atmospheric formaldehyde before TD-GC−MS determination (Figure 2a).[12] Atmospheric formaldehyde was simultaneously sampled and preconcentrated on a MOF-5 packed quartz tube, then thermally desorbed for GC-MS analysis. Formaldehyde was
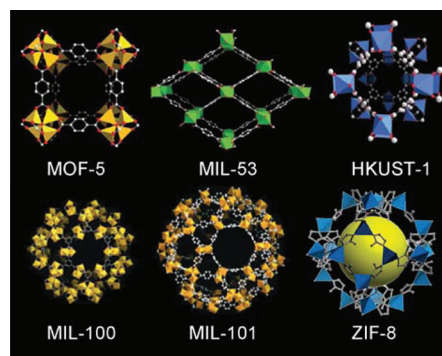

FIGURE 1. Structures of typical MOFs used in analytical chemistry. Adapted and reproduced with permission from refs 4, 42, and 43. Copyright 2008 Royal Society of Chemistry; Copyright 2008 and 2009 American Chemical Society.

likely adsorbed on zinc corner sites in MOF-5. MOF-5 provided substantial benefits for trapping formaldehyde in indoor and outdoor air with a relative humidity less than 45% (Figure 2b). The recovery of formaldehyde on MOF-5 was 95% even 24 h after sampling (Figure 2c), allowing the analysis of samples from rather remote areas, which necessitates a greater delay between sampling and analysis in the laboratory. Even if analysis was not possible on the same day, a recovery of 90% was still obtained even after 72 h storage at 20 °C (Figure 2c). One tube packed with 300 mg of MOF-5 lasted 200 cycles of adsorption/TD without significant loss of collection efficiency. This MOF-5 based approach provides a fast (<10 min), highly sensitive, and reproducible (2.8−5.3% relative standard deviation (RSD)) method for determination of atmospheric formaldehyde with wide linear range of 3 orders of magnitude and low detection limit of 0.6 μg m^{-3}. Porous MOF-5 with large surface area and zinc corner sites is much more favorable to the adsorption of formaldehyde than commercial sorbents Tenax TA and Carbograph 1TD.[12]

While bulk microsized MOFs are convenient for direct application to in-field sampling/trapping VOCs, engineered thin MOF films are suitable as novel coatings for sensitive smart devices to detect VOCs. The elegant marriage of MOFs and QCM offers an effective way for sensitive and selective detection of volatile targets.[13,40] Recently, we have employed a drop-coating method to fabricate thin MOF coatings on QCM crystals and designed a simple device for MOF-based QCM detection.[13] The developed device enables probing of the adsorption of volatile targets on MOFs at atmospheric pressure and around room temperature in N$_2$ atmosphere and provides a promising tool for characterizing MOFs. This MOF-based QCM system has been successfully applied to measure adsorption isotherms and monitor
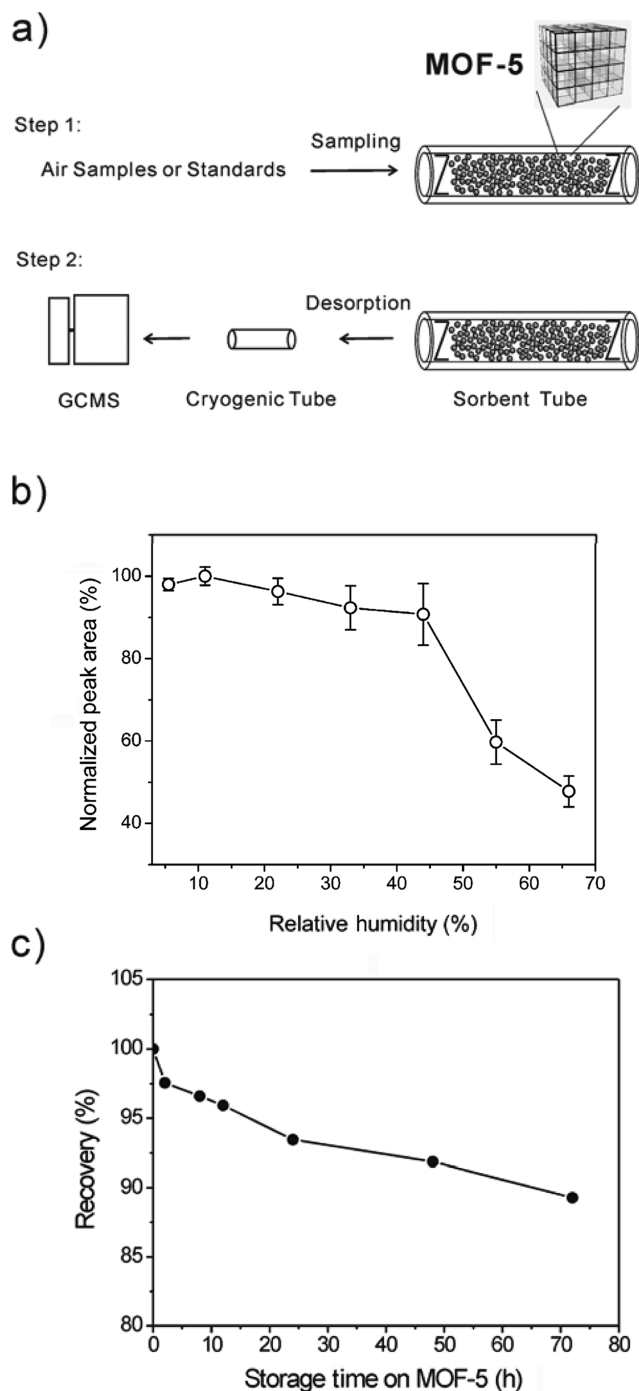
a)

MOF-5

Step 1:

Air Samples or Standards → Sampling → Sorbent Tube

Step 2:

GCMS ← Cryogenic Tube ← Desorption ← Sorbent Tube

b)

c)

FIGURE 2. (a) Sampling and desorption procedures on a MOF-5 packed tube, (b) effect of relative humidity on formaldehyde sampling, and (c) stability of formaldehyde adsorbed on MOF-5 in atmospheric air (30% relative humidity) at 20 °C. Reproduced with permission from ref 12. Copyright 2010 American Chemical Society.

dynamic processes for the adsorption of *n*-hexane, toluene, methanol, butanone, dichloromethane, and *n*-butylamine on MIL-101 (Figure 3). MIL-101 exhibited the strongest affinity and the most heterogeneous adsorption sites for *n*-butylamine but the weakest affinity and the most homogeneous adsorption

sites for *n*-hexane. The metal sites within the MIL-101 are vital in the adsorption process. MIL-101 gave much higher affinity and higher adsorption capacity than activated carbon to VOCs, offering great potential for real applications in the adsorption and removal of VOCs.[13]

MOFs for SPE and SPME

Besides in-field sampling and trapping, bulk microsized MOFs with good solvent stability are also promising as sorbents for SPE. In 2006, we demonstrated the application of MOFs as sorbent for SPE of PAHs in water samples.[14] Water-stable 2D copper(II) isonicotinate MOF was packed on a microcolumn for SPE online-coupled with HPLC. The copper(II) isonicotinate MOF is highly hydrophobic and water stable; thus it is a possible sorbent for extracting hydrophobic substances such as PAHs from aqueous solution. The enhancement factors of the PAHs depend on their shape, size, and hydrophobic properties, ranging from 200 to 2337 for naphthalene, phenanthrene, anthracene, fluoranthene, benzo(*b*)fluoranthene, benzo(*k*)fluoranthene, benzo(*a*)pyrene, and benzo(*ghi*)perylene.

MOFs are also attractive for efficient enrichment of low-abundance peptides and effective exclusion of high-abundance proteins from biological samples before MALDI-TOF-MS analysis. Such application is of great importance in peptidomics research, especially for discovering disease-associated biomarkers and elucidating biological and pathological variation. Recently, we have utilized MIL-53, MIL-100, and MIL-101 as sorbents to remove proteins and enrich peptides in biological fluids.[18] These MOFs have high surface area, large pores, and good chemostability and biocompatibility, and their different pore windows have resulted in different mass spectra patterns of the enriched peptides despite similar composition and topology of MIL-100 and MIL-101 (Figure 4c,e,g). Lower molecular weight peptides (<4200 Da) were effectively enriched on MIL-100 with the smallest pore window (5.6 and 8.6 Å), while larger molecular weight peptides (~8000 Da) were favorably trapped on MIL-53 with the largest pore window (17 Å). Besides, these MOFs showed good ability to exclude high-abundance proteins in human plasma (Figure 4). These observations have provided a view to molecule sieving effect of MOFs on nanometer scale for selective inclusion and exclusion of large biomolecules.[18]

Although bulk MOFs with microsized crystals are convenient as sorbents for direct application to SPE, thin films/coatings of MOFs are necessary for SPME application. For this
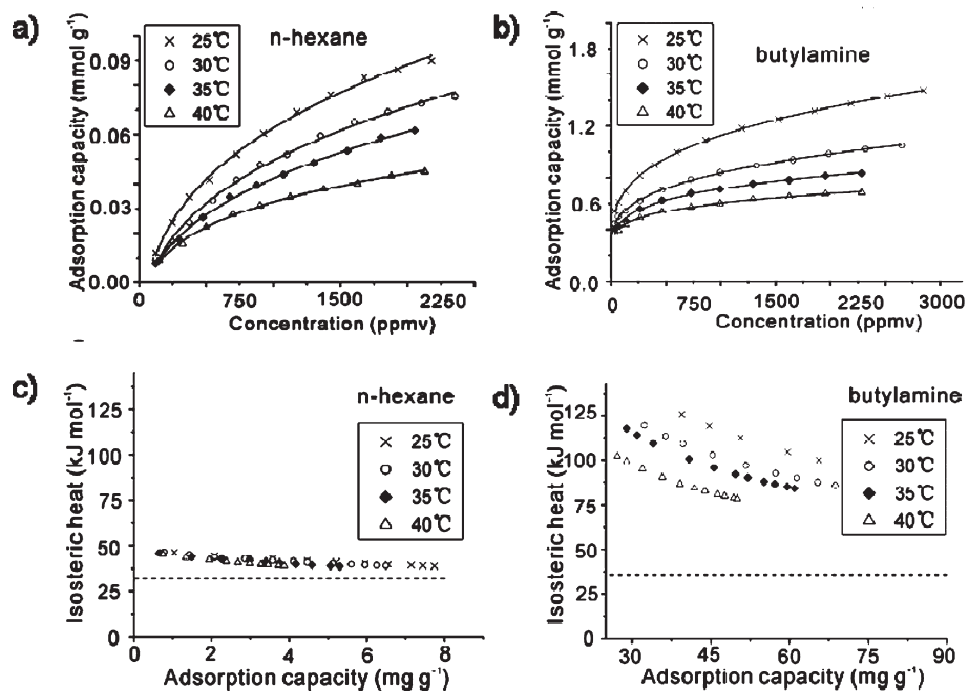
FIGURE 3. Adsorption isotherms of (a) hexane and (b) *n*-butylamine on MIL-101 measured by MIL-101-modified QCM device. Solid lines refer to fitted adsorption isotherms by Dubinin−Astakhov equation. Isosteric heats of adsorption for (c) hexane and (d) *n*-butylamine at different temperatures. The dashed lines refer to the enthalpy of vaporization of hexane at 25 °C. Adapted and reproduced with permission from ref 13. Copyright 2011 American Chemical Society.

reason, we have developed an in situ hydrothermal growth approach to fabricate thin coatings of MOF-199 on etched stainless steel wires.[19] The fabricated MOF-199 coated fibers were assembled into a homemade device for SPME of benzene homologues before GC−MS analysis (Figure 5a). The face-centered-cubic structure of MOF-199 contains three types of pores, of which two larger square-shaped pores (12 Å) penetrate the basic structure in all three dimensions and connect with pore windows of about 8.0 Å, providing selective extraction of analytes based on size-selectivity.[19,29,33] Meanwhile, MOF-199 possesses Lewis acid coordination sites on the interior of the pore walls, which greatly enhance the extraction ability based on electron-selectivity and make MOF-199 more selective for more electron-rich analytes.[19] Compared with commercial PDMS/DVB fibers, MOF-199 coated fiber gave much higher enhancement factors for the SPME of benzene homologues (Figure 5b). The MOF-199 coated fiber not only offered large enhancement factors from 19613 (benzene) to 110860 (*p*-xylene) but also exhibited wide linearity with 3 orders of magnitude, low detection limits of 8.3−23.3 ng L^{-1}, and good reproducibility of 2.0−7.7% (RSD) for benzene homologues. The excellent performance of MOF-199 coated fiber results from the combined effects of large surface area and

unique porous structure of MOF-199, $\pi-\pi$ interaction of the aromatic rings of analytes with the framework 1,3,5-benzenetricarboxylic acid molecules, and π-complexation of electron-rich analytes to the Lewis acid sites in MOF-199.[19]

MOFs as Stationary Phases for GC

Since the first application of bulk MOF-508 as stationary phase for packed column GC by Chen and co-workers,[20] a few other MOFs (MIL-47, MOF-5, and ZIF-8) have been also reported for packed column GC.[21−23] Because characterization of MOFs as stationary phases by polarity is important to screening MOFs for practical GC applications, we have applied McReynolds indices for the classification of MOFs to characterize MOF columns.[23] Two zinc-terephthalate MOFs (MOF-5 and MOF-monoclinic) with different structures were used as examples. On the basis of the measured McReynolds constants, MOF-5 was characterized as a nonpolar stationary phase, whereas MOF-monoclinic was characterized as an intermediate polar stationary phase for GC. Such classification of MOFs using McReynolds indices should be helpful for the development of their chromatographic applications.

Packed columns with bulk MOFs need gram-scale MOF and lead to low resolution and separation efficiency and
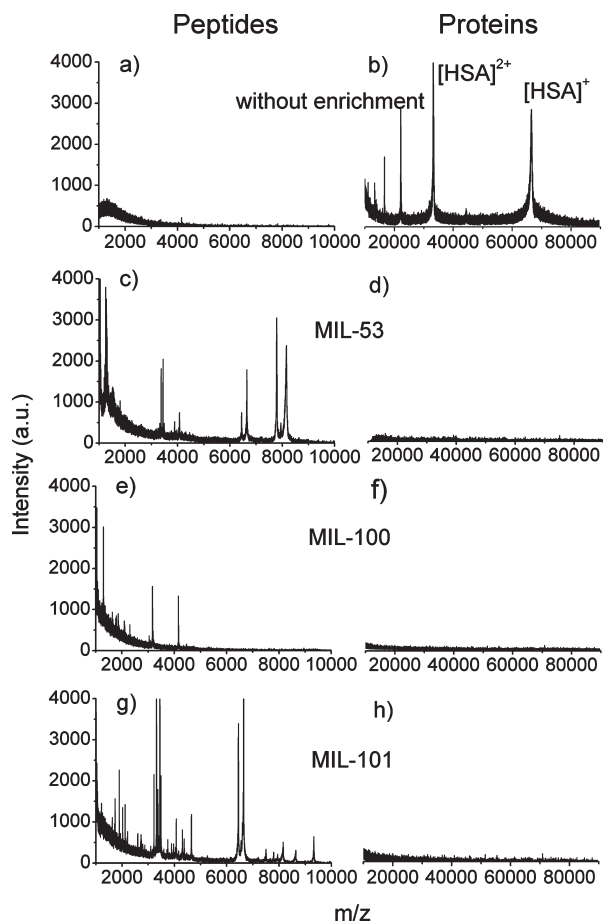
FIGURE 4. Mass spectra of human plasma obtained by MALDI-TOF-MS before enrichment (a, b) and after enrichment with MIL-53 (c, d), MIL-100 (e, f), and MIL-101 (g, h). Reproduced with permission from ref 18. Copyright 2011 Royal Society of Chemistry.

high-cost application of MOFs for GC. In contrast, the porous layer open tube (PLOT) capillary columns permit a thin film of MOFs coated on their inner walls to improve the resolving power of MOFs and to save the dosage of MOFs for GC applications.[24] For these reasons, we have employed a dynamic coating approach to fabricate the first MOF-coated capillary for high-resolution GC.[24] MIL-101 was taken as stationary phase due to its high surface area, large pores (29 and 34 Å), accessible open metal sites, and excellent chemical and thermostability. Important targets (xylene isomers and ethylbenzene (EB)) in industry and environmental sciences were used as the analytes. Although separation of xylene isomers and EB is challenging due to the similarity of their boiling points, MIL-101 coated capillary gave a baseline separation of *p*-xylene, *o*-xylene, *m*-xylene, and EB within 1.6 min without the need for temperature programming (Figure 6c). Such fast and high-resolution separation of xylene isomers and EB has rarely been observed on either
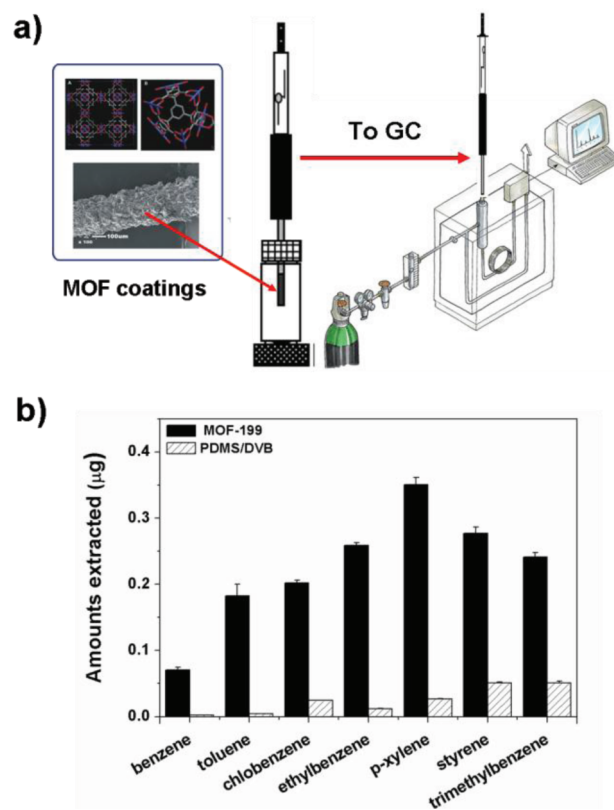

FIGURE 5. (a) Schematic for the application of MOF-coated fiber for SPME before GC analysis and (b) comparison of MOF-199 coated fiber with commercial PDMS/DVB fiber for SPME of benzene homologues: 3.6 μg L^{-1} for benzene, toluene, ethylbenzene, *p*-xylene, styrene, and trimethylbenzene and 4.6 μg L^{-1} for chlorobenzene. Adapted and reproduced with permission from ref 19. Copyright 2009 American Chemical Society.
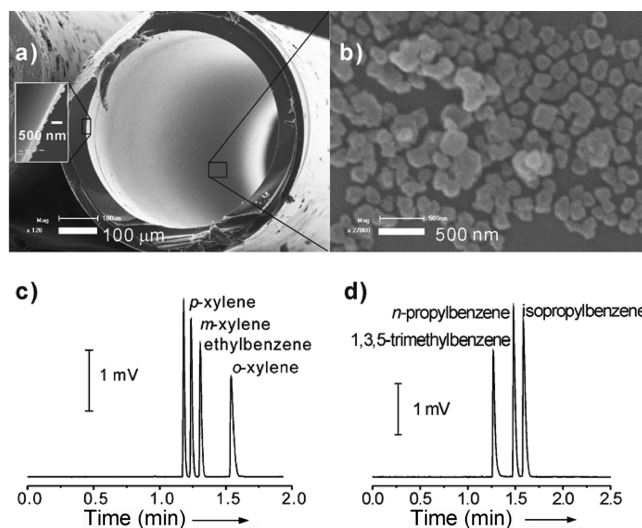

FIGURE 6. SEM images of (a) cross section of MIL-101 coated capillary and (b) MIL-101 deposited on the inner wall of the capillary and chromatograms on the MIL-101 coated capillary (15 m long × 0.53 mm i.d.) under a N$_2$ flow rate of 3 mL min^{-1} at 160 °C of (c) xylene isomers and EB (350 ng each) and (d) 1,3,5-trimethylbenzene, *n*-propylbenzene, and isopropylbenzene (1.0 μg each). Reproduced with permission from ref 24. Copyright 2010 Wiley-VCH.
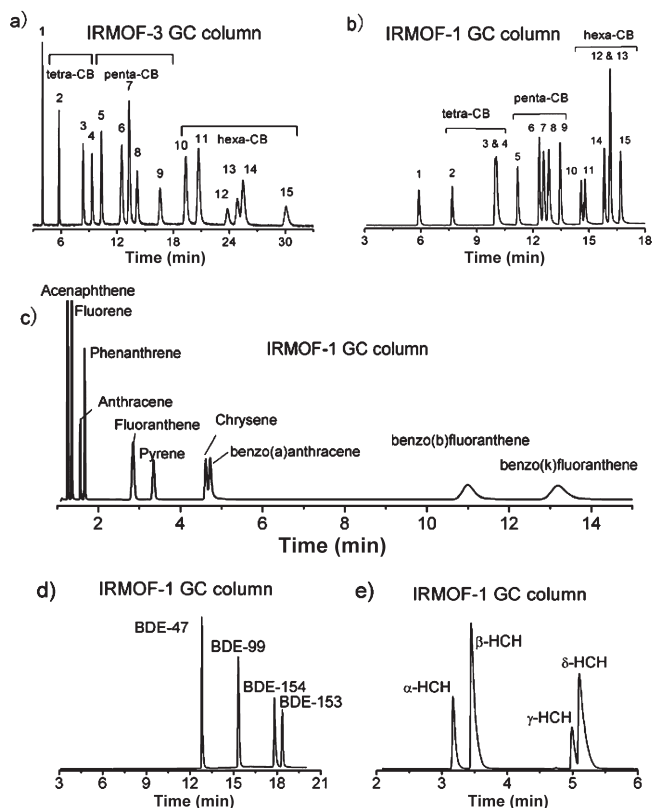
FIGURE 7. High-resolution separation of (a) 15 PCBs (1, PCB-281; 2, PCB-52; 3, PCB-77; 4, PCB-81; 5, PCB-101; 6, PCB-105; 7, PCB-118; 8, PCB-114; 9, PCB-126; 10, PCB-138; 11, PCB-153; 12, PCB-167; 13, PCB-156; 14, PCB-157; 15, PCB-169) on IRMOF-3 coated capillary (25 m long × 250 μm i.d.) at 280 °C, (b) PCBs on IRMOF-1 coated capillary (25 m long × 250 μm i.d.) using a three-step temperature program of 180 °C for 2 min, then 5 °C min^{-1} to 290 °C, and finally 290 °C, (c) PAHs on IRMOF-1 coated capillary (25 m long × 250 μm i.d.) at 300 °C, (d) PBDEs on IRMOF-1 coated capillary (25 m long × 250 μm i.d.) by a three-step temperature program of 180 °C for 2 min, then 5 °C min^{-1} to 310 °C, and finally 310 °C, and (e) HCH isomers on IRMOF-1-coated capillary using a three-step temperature program of 200 °C for 2 min, then 10 °C min^{-1} to 280 °C, and finally 280 °C. Reproduced with permission from ref 25. Copyright 2011 American Chemical Society.

previous packed MOF columns or other traditional capillary columns. The excellent selectivity of MIL-101 coated capillary originates not only from host–guest interactions but also from accessible open metal sites and suitable polarity of MIL-101.[24] MIL-101 coated capillary also allows high-resolution separation of other substituted benzene derivatives and a mixture of alkanes (Figure 6d).[24]

Because it is difficult to coat capillary with microsized MOFs synthesized conventionally, we have developed a 1 min, room-temperature approach for synthesizing nanosized isoreticular MOFs (IRMOFs).[25] Unlike other methods for preparing nanosized IRMOFs, this method does not require activation or usage of auxiliary stabilizing agents.
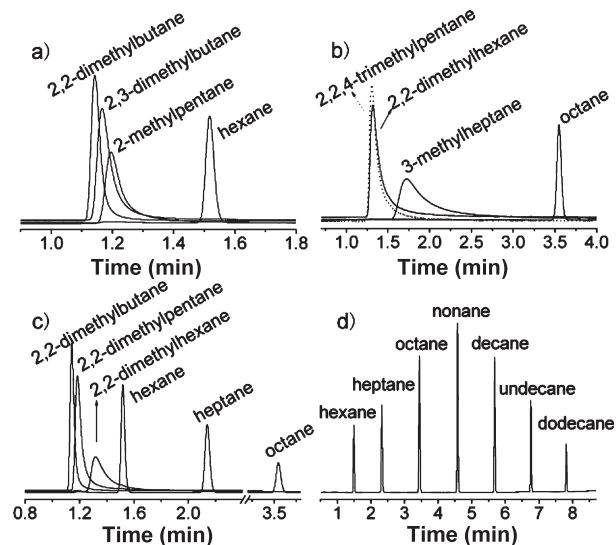

FIGURE 8. Chromatograms on ZIF-8 coated capillary (20 m long × 0.25 mm i.d.) for GC separation: (a) hexane and its branched isomers; (b) octane and its branched isomers; (c) 2,2-dimethyl-branched alkanes and linear alkanes at a N$_2$ flow rate of 1 mL min^{-1} under 170 °C; (d) linear alkanes at a N$_2$ flow rate of 1.5 mL min^{-1} using a temperature program of 140 °C for 1 min, then 20 °C min^{-1} to 290 °C. Reproduced with permission from ref 26. Copyright 2010 American Chemical Society.

The fabricated nanosized IRMOF-coated capillaries have been applied for successful high-resolution GC separation of polychlorinated biphenyls (PCBs), PAHs, polybrominated diphenylethers (PBDEs), and hexachlorocyclohexanes (HCHs) (Figure 7).[25] These targets are important groups of persistent organic pollutants (POPs) and have significant adverse impacts on human health and environment due to their toxicity, persistency, and bioaccumulation. Their separation is important for environmental research but challenging because of their high boiling points and similar chemical and physical properties. The fabricated IRMOF-coated capillaries showed high-resolution separation of POPs with good reproducibility, great column efficiency (2293 and 2063 plates m^{-1} for IRMOF-1 and IRMOF-3, respectively) and wide linear range with 3 orders of magnitude. In particular, the IRMOF-1 coated capillary offered a high-resolution separation of several intractable PAH isomer pairs, such as anthracene/phenanthrene and benzo-[*b*]fluoranthene/benzo[*k*]fluoranthene, though they are difficult to baseline-separate on commercial HP-5MS column.[25] The IRMOF-1 and IRMOF-3 coated capillaries also offered group separation of PCB isomers. Furthermore, IRMOF-3 (with amino ligand) exhibited stronger interaction with PCBs, higher polarity, and larger zero-coverage adsorption enthalpies than IRMOF-1 (without amino ligand).

The separation of linear alkanes from branched isomers is a very important process in petroleum refining to improve
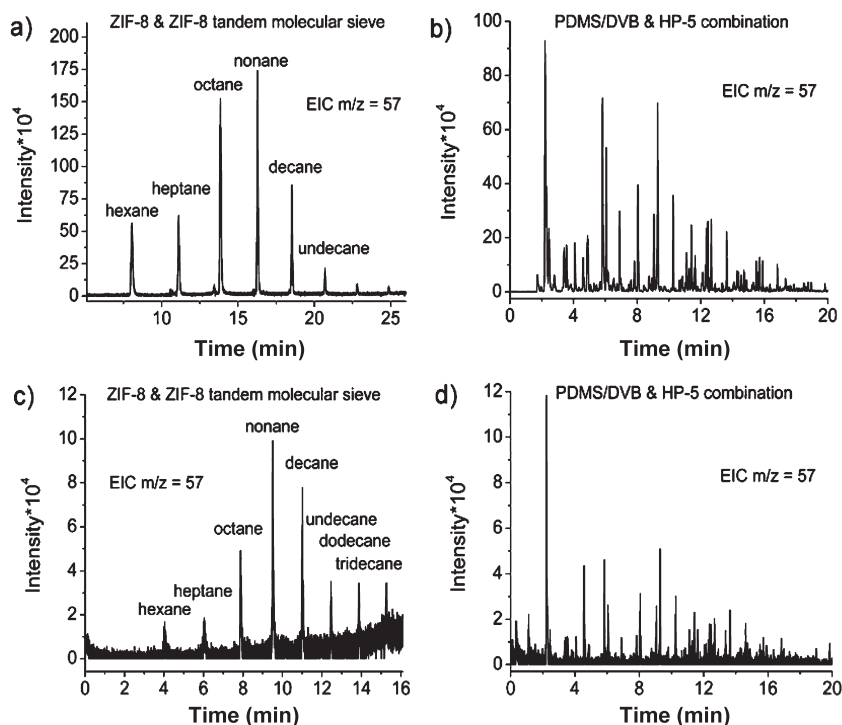
FIGURE 9. Extracted ion chromatograms (EICs) of a petroleum-based fuel (a, b) and human serum (c, d) using a tandem ZIF-8 molecular sieve platform (ZIF-8 based SPME followed by ZIF-8 based GC separation) (a, c), and a combination of PDMS/DVB SPME fiber with HP-5 capillary (30 m long × 0.25 mm i.d.) (b, d). GC separation: ZIF-8 coated capillary (20 m long × 0.25 mm i.d.) at a He flow rate of 1 mL min^{-1} using temperature programming (40 °C for 1 min, then 10 °C min^{-1} to 290 °C), and HP-5 capillary at a He flow rate of 1 mL min^{-1} using temperature programming (30 °C for 3 min, then 5 °C min^{-1} to 250 °C). Reproduced with permission from ref 29. Copyright 2011 American Chemical Society.

the gasoline octane number and the low-temperature properties of aviation fuels; thus the process and mechanism of such separations are always of great concern. Recently, we have explored ZIF-8 as molecular sieving materials and fabricated a ZIF-8 coated capillary for high-resolution separation of alkanes.[26] Owing to the narrow six-membered-ring pore windows (3.4 Å) and large pores (11.4 Å), the ZIF-8 coated capillary has a strong ability to separate linear alkanes from branched alkanes. Besides, the ZIF-8 coated capillary offers excellent features for high-resolution separation of linear alkanes due to van der Waals interaction between linear alkanes and the hydrophobic inner surfaces of the micropores (Figure 8).

Although PLOT columns are widely used for GC separation, very limited materials such as nanoparticles of alumina, carbon, silica, molecular sieve, and a few porous polymers are currently suitable as the coatings for PLOT columns. The large diversity in structure and pore size, high surface area, good thermostability and adsorption affinity of MOFs have provided great opportunity to fabricate various MOF-coated PLOT columns for wide applications (even chiral separation[27]) of high-resolution GC. Development of in situ growth techniques to produce firm chemically bonded thin films of MOFs on the inner walls of capillary columns is thus significant for promoting the practical applications of MOFs in high-resolution GC.[28]

MOF-Based Tandem Molecular Sieve as a Dual Platform for Analysis of Complex Samples

Although obvious molecular sieving effect has been observed in SPME and GC separation, effective separation of target analytes in complicated matrixes by individual MOF-based SPME or GC is still difficult because SPME procedure alone is hard to distinguish analytes with small difference in the interaction with the MOF coating while MOF-based GC alone is difficult to analyze complicated samples owing to the limited column capacity and selectivity.[19,26,29] However, an appropriate combination of MOF-coated fiber for SPME with MOF-coated capillary for GC separation provides an effective MOF-based tandem molecular sieve platform for selective microextraction and high-resolution GC separation of target analytes in complex samples.[29] An elegant combination of ZIF-8 coated fiber for SPME with ZIF-8 coated capillary for subsequent GC separation allows such dual platform for selective and efficient determination of volatile
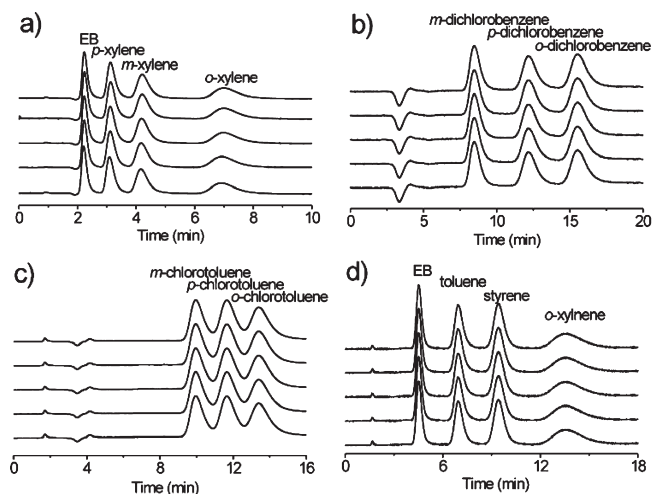
FIGURE 10. Chromatograms on MIL-101(Cr)-packed column (5 cm long × 4.6 mm i.d.) for five replicate separations: (a) EB and *p*-, *m*-, and *o*-xylene (5 μL, 1 g L^{-1} each) using hexane/dichloromethane (95:5) as mobile phase at 1 mL min^{-1}; (b) *m*-, *p*-, and *o*-dichlorobenzene (5 μL, 1 g L^{-1} each) using hexane/dichloromethane (90:10) as mobile phase at a flow rate of 0.5 mL min^{-1}; (c) *m*-, *p*-, and *o*-chlorotoluene (5 μL, 1 g L^{-1} each) using hexane/dichloromethane (95:5) as mobile phase at 0.5 mL min^{-1}; (d) EB, toluene, styrene, and *o*-xylene (5 μL, 1 g L^{-1} each) using hexane as mobile phase at 0.5 mL min^{-1}. UV detection at 254 nm. Reproduced with permission from ref 34. Copyright 2011 American Chemical Society.

FIGURE 11. (a) Chromatograms for 13 replicate separations of C_{60} and C_{70} and (b) separation of fullerenes in the toluene solution of carbon soot (2.63 mg mL^{-1}) on MIL-101(Cr) packed column (5 cm long × 4.6 mm i.d.) with dichloromethane/acetonitrile (98:2) as mobile phase at 1 mL min^{-1} with UV detection at 340 nm. Reproduced with permission from ref 36. Copyright 2011 Wiley-VCH.

n-alkanes in complex petroleum-based fuel and human serum samples (Figure 9). Moreover, the combination of ZIF-7 coated SPME fiber with MIL-101 coated capillary GC offers strong power to selectively extract benzene homologues and high-resolution separation of substituted benzene derivatives.[29] The large diversity in structure and pore size allows various combinations of MOFs for designing MOF-based tandem molecular sieve platforms to achieve different selectivity in extraction and chromatographic separation and to solve problems in complex real sample analysis.

MOFs as Stationary Phases for HPLC

Since the application of a glass tube column packed with a homochiral Zn–organic framework in LC by Fedin and co-workers,[30] several other MOFs (MIL-47, MIL-53, MOF-5, and HKUSK-1) have been reported for LC applications.[31−33,41] However, all the above-mentioned applications of MOFs in HPLC employ a single nonpolar or low polar solvent as mobile phase, even though the composition of mobile phase can play significant roles in retention, resolution, and selectivity. To explore the potential of MOFs for wide HPLC applications, we have employed binary or polar mobile phase for HPLC separation of substituted aromatics on MIL-101(Cr) packed column, and position isomers on
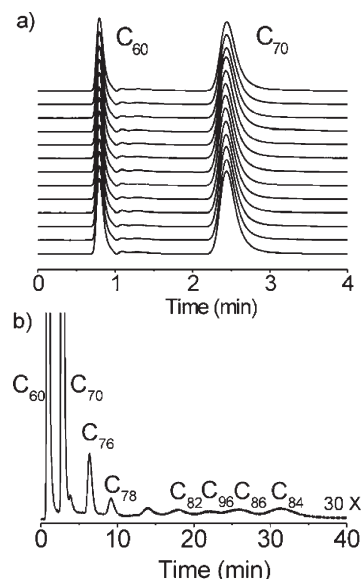
MIL-53(Al) packed column.[34,35] The use of hexane/dichloromethane as mobile phase enables MIL-101(Cr) packed column for baseline separation of EB and xylene, dichlorobenzene, and chlorotoluene isomers and EB and styrene with high column efficiency (20000 plates m^{-1} for EB) and excellent precision (<2.9% RSD) (Figure 10). The MIL-101(Cr) packed column offers high affinity for the *ortho*-isomer, allowing fast and selective separation of *ortho*-isomer from other isomers within 3 min.[34] The separation of xylene, dichlorobenzene, and chlorotoluene on MIL-101(Cr) is controlled by entropy change, while the separation of EB and styrene on MIL-101(Cr) is governed by enthalpy change.[34] Moreover, the combination of hexane/dichloromethane or dichloromethane/methanol binary mobile phase with MIL-53(Al) packed column also gives reproducible and high-resolution separations of xylene, dichlorobenzene, chlorotoluene, and nitrophenol isomers based on entropy change control.[35]

MOFs are also promising materials for selective HPLC separation of fullerenes. Recently, we have applied MIL-101(Cr) packed column in combination with dichloromethane/acetonitrile (98:2) as mobile phase to high-resolution separation of fullerenes.[36] C_{60} and C_{70} were separated on MIL-101(Cr) packed column at room temperature within 3 min with excellent selectivity ($\alpha(C_{70}/C_{60})$ = 17), much better than those ($\alpha(C_{70}/C_{60})$ = 1.5−7) obtained on previous
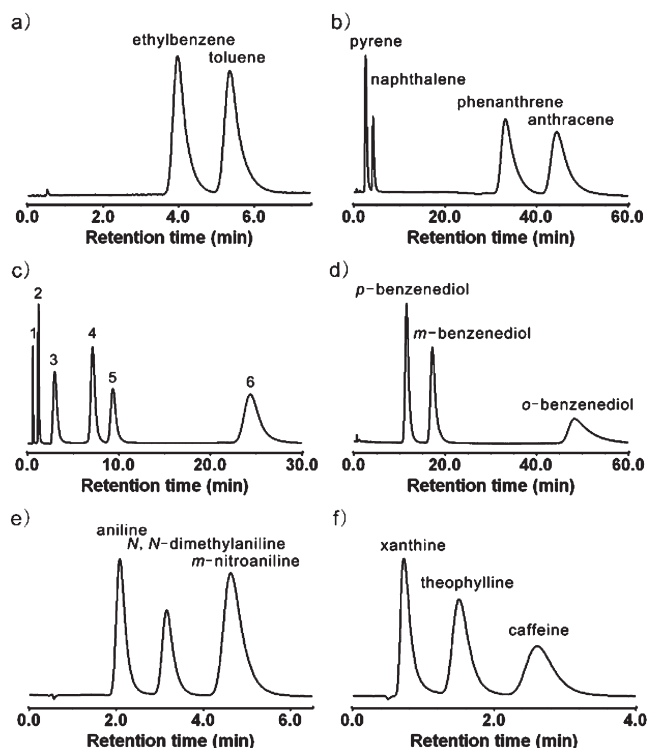
FIGURE 12. Chromatograms on MIL-53(Al) packed column (7 cm long × 4.6 mm i.d.) forRP-HPLC separation using CH_3CN/H_2O as mobile phase at 1.0 mL min^{-1}: (a) EB and toluene; (b) PAHs; (c) thiourea (1), phenol (2), aniline (3), benzaldehyde (4), bromobenzene (5), and naphthalene (6); (d) o-benzenediol, m-benzenediol, and p-benzenediol; (e) aniline, N,N-dimethylaniline, and m-nitroaniline; (f) xanthine, theophylline, and caffeine. Mobile phase composition (CH_3CN/H_2O, v/v): (a) 7:3; (b) 10:0; (c) 6:4; (d) 1:9; (e) 9:1; (f) 5:5. UV detection at 210 nm (a, c), 256 nm (b), 70 nm (f), and 280 nm (d, e). Reproduced with permission from ref 39. Copyright 2012 Royal Society of Chemistry.

stationary phases^{36}), high column efficiency (13000 plates m^{-1} for C_{70}), and good reproducibility (<1.7% RSD) (Figure 11a). MIL-101(Cr) packed column also gave a high-resolution separation of other high fullerenes such as C_{76}, C_{78}, C_{82}, C_{84}, C_{86}, and C_{96} (Figure 11b). The excellent selectivity of MIL-101(Cr) likely results from the difference in the solubility of fullerenes in mobile phase, diffusion of fullerenes through the pores of MIL-101(Cr), and $\pi−\pi$ and van der Waals interactions between fullerenes and the inner walls of the pores of MIL-101(Cr).^{36}

Exploring the potential of MOFs in reversed-phase (RP) HPLC applications (with a binary mixture of water and a miscible polar organic solvent as mobile phase) is of great significance because RP-HPLC is the most widely used technique for separation in life and environmental sciences and biomedical research. However, publications on the application of MOFs for RP-HPLC have been very limited so far. The prerequisite for HPLC application is that the MOFs should

have good stability in the RP mobile phase of H_2O/CH_3CN or H_2O/CH_3OH. In a proof-of-concept study,^{39} we have explored MIL-53(Al) as a model RP stationary phase because it is a three-dimensional framework with one-dimensional lozenge-shaped pore channels with aromatic ring walls, high surface area, suitable crystal size, and excellent chemical and solvent stability. MIL-53(Al) packed column allows RP-HPLC separation of a wide range of analytes from nonpolar to polar and acidic to basic solutes with good resolution, selectivity, stability, and reproducibility (Figure 12). This work may open a new avenue for broad applications of MOFs in RP-HPLC separation.

The unique features of high porosity, shape selectivity, and multiple active sites give MOF-packed columns greater potential for HPLC based on the combined mechanisms of size-exclusion, shape selectivity, and hydrophobicity than C_{18} columns.^{39} However, current MOF-packed columns give lower column efficiency than commercial C_{18} column due to large particle size distribution and irregular shape of the prepared MOFs.^{39} It is thus imperative to fabricate uniform spherical particles of MOFs or MOF composites^{37} to improve column efficiency for HPLC.

Conclusion and Outlook

In this Account, we have summarized our recent achievements on MOFs for analytical chemistry. The analytical applications of MOFs have covered most important aspects of modern analytical chemistry. All of the analytes targeted are of environmental, biological, or industrial significance. Also, MOFs have been engineered to specific forms such as columns, fibers, and films to meet various analytical challenges and to improve analytical sensitivity and selectivity.

There is still great room for further exploration of MOFs for analytical applications. Moisture, water, or other solvent stable MOFs are needed not only in the applications in humid atmosphere but also in environmental and biological related research for the analysis of pollutants and biomolecules in aqueous solution. Precise control for engineering MOFs to films, 2D patterns, and 3D structures is necessary for facilitating the fabrication of smart multifunctional devices to explore the practical applications and to meet analytical challenges for biological and environmental research. Combination of MOF and other materials to build multifunctional composites such as MOF/nanoparticles, MOF/graphene, MOF/silica, and MOF/organic polymers is also a solution to improving analytical performance. In the near future, great effort should be made to explore more practical analytical uses of MOFs, to make full use of currently available MOFs

to solve analytical problems, and to design specific MOFs for special analytical challenges.

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FOOTNOTES

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